



US007566539B2

(12) **United States Patent**
LaRosa

(10) **Patent No.:** US 7,566,539 B2
(45) **Date of Patent:** Jul. 28, 2009

(54) **ANTI-CCR2 ANTIBODIES AND METHODS OF USE THEREFOR**(75) Inventor: **Gregory J LaRosa**, Newton, MA (US)(73) Assignee: **Millennium Pharmaceuticals, Inc.**, Cambridge, MA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 353 days.

(21) Appl. No.: **10/656,805**(22) Filed: **Sep. 5, 2003**(65) **Prior Publication Data**

US 2005/0048052 A1 Mar. 3, 2005

Related U.S. Application Data

(63) Continuation of application No. 09/898,513, filed on Jul. 3, 2001, now abandoned, which is a continuation of application No. 09/121,781, filed on Jul. 23, 1998, now Pat. No. 6,312,689.

(51) **Int. Cl.****G01N 33/53** (2006.01)**G01N 33/567** (2006.01)**G01N 33/574** (2006.01)**C07K 17/00** (2006.01)(52) **U.S. Cl.** **435/7.1; 435/7.2; 435/7.21;**
..... **435/7.23**(58) **Field of Classification Search** None
See application file for complete search history.(56) **References Cited**

U.S. PATENT DOCUMENTS

4,816,397 A	3/1989	Boss et al.
4,816,567 A	3/1989	Cabilly et al.
5,225,539 A	7/1993	Winter
5,440,021 A	8/1995	Chuntharapai et al.
5,543,503 A	8/1996	Chuntharapai et al.
5,571,713 A	11/1996	Lyle et al.
5,585,089 A	12/1996	Queen et al.
5,657,277 A	8/1997	Shirley
5,693,761 A	12/1997	Queen et al.
5,693,762 A	12/1997	Queen et al.
5,707,815 A	1/1998	Charo et al.
5,808,960 A	9/1998	McClure
5,858,089 A *	1/1999	Martinovic 118/13
5,859,205 A	1/1999	Adair et al.
5,985,279 A	11/1999	Waldmann et al.
6,006,339 A	12/1999	McClure
6,075,181 A *	6/2000	Kucherlapati et al. 800/25
6,084,075 A *	7/2000	Lind et al. 530/388.22
6,312,689 B1	11/2001	LaRosa
6,352,832 B1	3/2002	LaRosa et al.
6,395,497 B1	5/2002	LaRosa
6,406,694 B1	6/2002	LaRosa
6,406,865 B2	6/2002	LaRosa
6,448,021 B1	9/2002	LaRosa
6,451,522 B2	9/2002	LaRosa
6,458,353 B1	10/2002	LaRosa
6,491,915 B2	12/2002	LaRosa

6,696,550 B2	2/2004	LaRosa et al.
7,053,202 B2	5/2006	O'Keefe et al.
2003/0165494 A1	9/2003	LaRosa et al.
2004/0126851 A1	7/2004	LaRosa et al.
2004/0132980 A1	7/2004	LaRosa et al.
2004/0151721 A1	8/2004	O'Keefe et al.
2004/0265303 A1	12/2004	LaRosa et al.
2006/0147445 A1	7/2006	O'Keefe et al.

FOREIGN PATENT DOCUMENTS

WO	WO 91/09967	7/1991
WO	WO 94/09128	4/1994
WO	WO 94/12214	6/1994
WO	WO 95/08576	3/1995
WO	WO 95/19436	7/1995
WO	WO 97/31949	* 9/1997
WO	WO 97/47319	12/1997
WO	WO 98/42360	10/1998
WO	WO 98/44953	10/1998
WO	WO 99/15666	4/1999
WO	WO 00/05265	2/2000

OTHER PUBLICATIONS

Lederman et al. Molecular Immunology. 1991. 28(11):1171-1181.*
Li et al. PNAS. 1980. 77(6):3211-3214.*

Frade et al. The Journal of Immunology 1997, 159:5576-5584.*

Li et al. Biochemistry 2000. 39:6296-6309.*

Förster, R., et al., "A general method for screening mAbs specific for G-protein coupled receptors as exemplified by using epitope tagged BLR1-transfected 293 cells and solid-phase cell ELISA", *Biochemical and Biophysical Research Communications*, 196(3):1496-1503 (1993).Boring, L., et al., "Decreased lesion formation in CCR2^{-/-} mice reveals a role for chemokines in the initiation of atherosclerosis," *Nature*, 394(27):894-897 (1998).Ylä-Herttuala, S., et al., "Expression of monocyte chemoattractant protein 1 in macrophage-rich areas of human and rabbit atherosclerotic lesions," *Proc. Natl. Acad. Sci., USA*, 88:5252-5256 (1991).Taubman, M.B., et al., "JE mRNA Accumulates Rapidly in Aortic Injury and in Platelet-Derived Growth Factor-Stimulated Vascular Smooth Muscle Cells," *Circulation Research* 70(2): 314-325 (1992).Feng, A., et al., "Red Wine Inhibits Monocyte Chemoattractant Protein-1 Expression and Modestly Reduces Neointimal Hyperplasia After Balloon Injury in Cholesterol-Fed Rabbits," *Circulation* 100:2254-2259 (1999).

(Continued)

Primary Examiner—Maher M Haddad

Assistant Examiner—Chun Dahle

(74) Attorney, Agent, or Firm—Lando & Anastasi, LLP

(57) **ABSTRACT**

The present invention relates to an antibody or functional fragment thereof which binds to a mammalian (e.g., human) CC-chemokine receptor 2 (CCR2) or a portion of the receptor and blocks binding of a ligand to the receptor. The invention further relates to a method of inhibiting the interaction of a cell bearing mammalian CCR2 with a ligand thereof, and to use of the antibodies and fragments in therapeutic, prophylactic and diagnostic methods.